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| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 2470 | chemotherapy same (side adj effect) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:12 | | | 0 |
| 2 | BRS | L2 | 2930 | angiotensinogen or (angiotensin adj I) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:13 | | | 0 |
| 3 | BRS | L3 | 5440 | angiotensin adj II | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:13 | | | 0 |
| 4 | BRS | L4 | 1 | (chemotherapy same (side adj effect)) same (angiotensinogen or (angiotensin adj I) or (angiotensin adj II)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:14 | | | 0 |
| 5 | BRS | L6 | 33544 | (hematopoietic adj toxicity) or (hematopoietic adj progenitor adj cell) or anemia or myelosuppression or pancytopenia or thrombocytopenia or neutropenia or lymphopenia or leukopenia or stomatitis or alopecia or headache or (muscle adj pain) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:18 | | | 0 |
| 6 | BRS | L7 | 267 | 1 same 6 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:19 | | | 0 |
| 7 | BRS | L8 | 0 | 7 same (2 or 3) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:19 | | | 0 |
| 8 | BRS | L9 | 2406 | 6 same chemotherapy | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:20 | | | 0 |
| 9 | BRS | L10 | 5 | 9 same (2 or 3) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:20 | | | 0 |
| 10 | BRS | L11 | 26027 | cytokine | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:25 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 11 | BRS | L12 | 832355 | (granulocyte adj colony adj stimulating adj factor) or (granulocyte adj macrophage adj csf) or (epidermal adj growth adj factor) or interleukin or thrombopoietin or (growth adj factor) or pixkines or (stem adj cell factor) or (flt adj ligand) or (megakaryocyte adj development) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:33 | | | 0 |
| 12 | BRS | L13 | 1075 | (2 or 3) same (11 or 12) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:34 | | | 0 |
| 13 | BRS | L14 | 0 | 13 same 1 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:35 | | | 0 |
| 14 | BRS | L15 | 4 | 13 same chemotherapy | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:37 | | | 0 |
| 15 | BRS | L16 | 2 | 5326776.pn. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:38 | | | 0 |
| 16 | BRS | L17 | 2 | 5629292.pn. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:38 | | | 0 |
| 17 | BRS | L18 | 2 | 5824696.pn. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:39 | | | 0 |
| 18 | BRS | L19 | 51 | rodgers adj kathleen.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:40 | | | 0 |
| 19 | BRS | L20 | 64 | dizerega adj gere.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:40 | | | 0 |
| 20 | BRS | L21 | 1 | (19 or 20) and 11 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/18 11:40 | | | 0 |

=> d his

(FILE 'HOME' ENTERED AT 11:46:29 ON 18 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
11:46:54 ON 18 FEB 2003
L1 18020 S CHEMOTHERAPY (P) (SIDE EFFECT)
L2 297996 S ANGIOTENSINOGEN OR ANGIOTENSIN
L3 3606 S L2 (P) (FRAGMENT)
L4 29 S L1 (P) L2
L5 0 S L1 (P) L3
L6 17 DUPLICATE REMOVE L4 (12 DUPLICATES REMOVED)
L7 321749 S (HEMATOPOIETIC TOXICITY) OR (HEMATOPOIETIC PROGENITOR CELL) O
L8 381376 S THROMBOCYTOPENIA OR NEUTROPENIA OR LYMPHOPENIA OR LEUKOPENIA
L9 1085 S L2 (P) (L7 OR L8)
L10 12 S L3 (P) (L7 OR L8)
L11 9 DUPLICATE REMOVE L10 (3 DUPLICATES REMOVED)
L12 9 S L11 NOT L6
L13 691294 S CYTOKINE OR (GRANULOCYTE COLONY STIMULATING FACTOR) OR (GRANU
L14 1296395 S INTERLEUKIN OR THROMBOPOIETIN OR (GROWTH FACTOR) OR PIXKINES
L15 3 S (L6 OR L12) (P) (L13 OR L14)

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FILE 'MEDLINE' ENTERED AT 11:46:54 ON 18 FEB 2003

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FILE 'AGRICOLA' ENTERED AT 11:46:54 ON 18 FEB 2003

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=> s chemotherapy (p) (side effect)
L1        18020 CHEMOTHERAPY (P) (SIDE EFFECT)

=> s angiotensinogen or angiotensin
L2       297996 ANGIOTENSINOGEN OR ANGIOTENSIN

=> s l2 (p) (fragment)
L3         3606 L2 (P) (FRAGMENT)

=> s l1 (p) l2
L4           29 L1 (P) L2

=> s l1 (p) l3
L5            0 L1 (P) L3

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L4
L6            17 DUPLICATE REMOVE L4 (12 DUPLICATES REMOVED)

=> d l6 1-17 ibib abs

L6   ANSWER 1 OF 17  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   2000169962  EMBASE
TITLE:              Neoral use in the cardiac transplant recipient.
AUTHOR:             Valantine H.
CORPORATE SOURCE:   Dr. H. Valantine, Stanford University Hospital, CVRC,
                    Heart/Lung Transplantation Division, Palo Alto, CA 94305,
                    United States
SOURCE:             Transplantation Proceedings, (2000) 32/3 SUPPL. 1
                    (27S-44S).
                    Refs: 80
                    ISSN: 0041-1345  CODEN: TRPPA8
PUBLISHER IDENT.:   S 0041-1345(00)00862-9
COUNTRY:            United States
DOCUMENT TYPE:      Journal; General Review
FILE SEGMENT:       009     Surgery
                    018     Cardiovascular Diseases and Cardiovascular Surgery
                    037     Drug Literature Index
                    038     Adverse Reactions Titles
                    039     Pharmacy
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Special Considerations in the Cardiac Transplant Patient: CyA is the core
     immunosuppressant of choice for the majority of transplant patients. The
     introduction of Neoral, a new microemulsion formulation of CyA, and more
     recently a range of adjunctive immunosuppressants have further enhanced
     the efficacy and tolerability of CyA-based immunosuppression. In the first
     year following transplantation the major causes of morbidity and death are
     graft failure, acute rejection, and systemic infection. Patients with
     deteriorated pulmonary circulation before transplantation are at increased
     risk of early postoperative death. Risk factors for early acute rejection
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include female donor sex, young donor age, and multiple HLA-DR mismatches. The principal cause of death in the long term is graft vasculopathy which accounted for 40% of all deaths. Risk factors that have been hypothesized to play a role in the pathogenesis of graft vasculopathy 4 include hyperlipidemia, recipient age and gender, donor age, the number of HLA AB and DR mismatches, and CMV infection. Strategies proposed to reduce the risk of graft vasculopathy include aggressive use of lipid-lowering agents, avoidance of low CyA doses, and the use of adjunctive rapamycin or RAD therapy. Rejection surveillance therefore relies on routine serial endomyocardial biopsy. Recent research suggests that a more accurate assessment of the state of the graft can be obtained by considering the results across a number of biopsy samples obtained from different parts of the heart, rather than basing clinical judgment on the worst single result obtained. New molecular markers such as granzyme A mRNA are likely to improve the power of histology to diagnose and predict rejection. Neoral Immunosuppression in De Novo Patients: Neoral pharmacokinetics give greater bioavailability and less intrapatient variability than Sandimmune. In the keynote OLN 351 study comparing Neoral with Sandimmune in de novo heart transplant recipients, fewer Neoral patients needed antilymphocyte therapy to treat rejection, fewer female patients had rejection episodes in the Neoral group, the tolerability of the two formulations was equivalent, and there was a lower incidence of infections in the Neoral group. The clinical impact of Neoral in comparison with Sandimmune in de novo heart transplant patients has been investigated in a number of additional trials, including long-term studies, which have confirmed that Neoral is associated with: Lower CyA doses than Sandimmune. Equal or greater antirejection efficacy than Sandimmune. Comparable tolerability to Sandimmune. During the administration of intravenous CyA as an induction therapy in the days immediately following transplantation, there is evidence to suggest that a 6-hour infusion given twice daily, which mimics the pharmacokinetic profile of oral dosing, may be clinically more effective than a continuous 24-hour infusion. Neoral Immunosuppression in the Maintenance Patient: Milligram-for-milligram dose conversion from Sandimmune to Neoral is feasible. Following conversion, a reduction in the CyA dose may be required in the majority of patients to maintain target levels. In pediatric patients, the rate of elimination of CyA is greater and bioavailability increases with increasing age. Younger patients (less than 8 years of age) may be managed more effectively with a 3-times-daily, rather than a twice-daily dosing schedule. A number of studies have compared the clinical effects of Sandimmune and Neoral in maintenance therapy for cardiac transplant patients. As with de novo patients, these studies have found the new formulation of CyA to be associated with lower rates of acute rejection, lower therapeutic doses, and comparable tolerability. Milligram-to-milligram conversion from the old to the new CyA formulation is generally well tolerated, although in a minority of patients there is a significant increase in CyA levels. These may be associated with a transient increase in ***side*** ***effects*** which resolve on dose reduction. There is a dose-sparing effect with Neoral. Routine monitoring of both CyA and serum creatinine levels are advisable to optimize the tolerability and safety of therapy. Recent research indicates that drug monitoring 2 hours after CyA dosing provides a more accurate indication of AUC than trough level measurements. Patients with persistently low CyA levels are likely to be at increased risk of graft loss due to both acute rejection and chronic graft vasculopathy. New evidence suggests the use of C-2 CyA level monitoring to determine whether adequate drug is being absorbed. This TDM approach is not only recommended as a diagnostic tool but as a method for optimising Neoral immunosuppression. Long-term ***Side*** ***Effects*** of CyA Therapy: The major long-term safety problems directly associated with CyA-based immunosuppression include nephrotoxicity, hypertension, diabetes mellitus, and PTLD. CyA nephrotoxicity No clear risk factors for CyA nephrotoxicity have been identified and no correlation has been observed between CyA levels and serum creatinine levels. Overactivation of the renin- ***angiotensin*** system may play a role in the development of CyA nephrotoxicity, in which case early introduction of an ACE inhibitor would be expected to be of benefit. This possibility has yet to be investigated in a clinical trial. Reducing the CyA dose to treat renal dysfunction should be carried out with care, because this increases the risk of acute rejection. The introduction of additional, non- nephrotoxic adjunctive therapies such as MMF should be considered when substantially reducing the CyA dose. Hypertension: Management of hypertension requires careful attention to dietary sodium intake. Reducing the dose of CyA - as

well as steroids, which also contribute to the problem - is important although care must be taken to avoid increasing the risk of rejection. The use of nonsteroidal anti-inflammatory agents should be avoided in hypertensive patients receiving CyA, because this may lead to further impairment of renal function. Because hypertension is often at its greatest in the early morning in cardiac transplant patients and the normal diurnal variation in blood pressure is absent, optimal management is often achieved by giving larger doses of antihypertensive agents at bedtime. PTLD: The optimal treatment for PTLD has not yet been determined, but strategies involving a reduction of immunosuppression in combination with aggressive ***chemotherapy*** have reported significant success. Prophylactic use of antiviral therapy is also recommended. Diabetes and Steroid Withdrawal: Steroid-sparing protocols are an important strategy for reducing posttransplant diabetes and should especially be considered in patients judged on the basis of preoperative metabolic parameters to be at a high risk of developing diabetes. Although steroid-sparing protocols are undoubtedly beneficial to many patients receiving immunosuppression with CyA or other agents, there is continuing debate over the clinical benefits of complete steroid withdrawal. Adjunct Immunosuppression Agents: Although CyA remains the cornerstone of maintenance immunosuppression therapy, the use of new adjunctive agents can reduce the risk of rejection; enable lower, better-tolerated doses of CyA and steroids to be administered; and enable therapy to be better tailored to clinical needs. Simulect (basiliximab) and daclizumab induction therapy within a CyA-based protocol has been shown to be highly effective in reducing the incidence of early acute rejection episodes in two major trials in renal transplantation, and similar results are anticipated in heart transplantation. Substitution of MMF for azathioprine reduces the frequency and severity of acute rejection episodes, may delay the development of chronic graft vasculopathy, and may improve patient survival in CyA-treated heart transplant patients. Sirolimus (rapamycin) and RAD have complementary mode of action to CyA. Early indications are that they offer significant clinical benefits in heart transplantation, including reduced rejection rates, lower CyA toxicity through reduced doses, and possibly a reduced incidence of chronic graft vasculopathy. Tacrolimus has a similar mode of action to CyA and the two agents should not be used in combination. In terms of clinical outcomes, no clear advantage has been demonstrated for either agent in comparison with the other. However, in some circumstances it may be appropriate to switch patients from CyA to tacrolimus-based therapy or vice versa, either to treat refractory rejection in CyA patients, or to treat severe tacrolimus toxicity. A range of options is available for the treatment of acute rejection; these options vary according to rejection severity and persistence. Many of these use adjunctive immunosuppressants including MMF, rapamycin, or RAD.

L6 ANSWER 2 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999432608 MEDLINE
DOCUMENT NUMBER: 99432608 PubMed ID: 10502990
TITLE: Effective milrinone therapy to a Duchenne muscular dystrophy patient with advanced congestive heart failure.
AUTHOR: Matsumura T; Saito T; Miyai I; Nozaki S; Kang J
CORPORATE SOURCE: Department of Neurology, Toneyama National Hospital, Japan.
SOURCE: RINSHO SHINKEIGAKU. CLINICAL NEUROLOGY, (1999 Jun) 39 (6) 643-8.
Journal code: 0417466. ISSN: 0009-918X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991026

AB We experienced a Duchenne muscular dystrophy (DMD) patient with severe congestive heart failure (CHF) successfully treated with milrinone. He had been diagnosed as having CHF since 24 years of age when he began to have mechanical ventilation with a nasal mask at home. Although ***angiotensin*** converting enzyme (ACE) inhibitor was effective for his CHF, cardiac function worsened year by year. Respiratory infection triggered the exacerbation of CHF at the end of 1997 (27 years old). On admission to our hospital on January 7, 1998, PaO2 was 48 mmHg and

cardiothoracic ratio (CTR) was 62%. Both ventricles were dilated and ventricular wall motility was markedly reduced on ultrasonocardiography. Ejection fraction of the left ventricle (LVEF) was 5%. Serum brain natriuretic peptide (BNP) was 760 pg/ml. Continuous intravenous infusion of milrinone was started on January 8 at the rate of 0.25-0.35 microgram/kg/min. His general condition improved and LVEF increased up to 15% on January 27. No serious ***side*** ***effects*** were observed. Even after milrinone withdrawal, his cardiac condition remained stable until the end of February 1998. Temporary deteriorated CHF due to urinary tract infection was successfully treated by ***chemotherapy*** and milrinone. Subsequently he was discharged on March 13 and could stay in his home for 7 weeks uneventfully with milrinone infusion therapy. When he was readmitted to the hospital for evaluation of CHF on April 30, CTR was 44%, LVEF was 20% and BNP was 44 pg/ml. CHF is one of the life threatening complications for DMD. Although catecholamine is a well utilized agent for advanced CHF, it has limited effect in DMD, because beta receptors are down-regulated due to long-lasting cardiac dysfunction. Increased heart rate and arrhytmia are also serious problems during catecholamine therapy. Milrinone is a type III phosphodiesterase inhibitor having inotropic and vasodilatic actions with modest increase of heart rate and little torelance. Milrinone is probably effective in improving CHF of DMD and has less ***side*** ***effects*** as compared to catecholamine. We concluded that milrinone might improve quality of lives of DMD patients with advanced CHF, although further cumultative studies are necessary to confirm its effectiveness and safety.

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:438670 CAPLUS
DOCUMENT NUMBER: 129:92270
TITLE: Clinical study on xenon-enhanced CT and its methodological consideration
AUTHOR(S): Hyotani, Genhachi
CORPORATE SOURCE: Dep. Neurol. Surg., Wakayama Med. Coll., Wakayama, 640-0000, Japan
SOURCE: Wakayama Igaku (1998), 49(2), 223-233
CODEN: WKMIAO; ISSN: 0043-0013
PUBLISHER: Wakayama Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Following studies were performed to examine the hemodynamics of brain tumors, which seems to be useful to det. the appropriate adjuvant therapy; (1) basic study to establish the methodol. of the xenon-enhanced CT (Xe-CT), (2) measurement of the blood flow in and around the brain tumors, (3) blood flow changes under the induced hypertension. An appropriate time of xenon inhalation and the reproducibility of the examn. were detd. in 8 volunteers. Also, inadvertent effects of Xe-CT were studied in 428 times examn. The min. inhalation time to obtain the reliable and reproducible data was 4 min. Major ***side*** ***effects*** were not encountered, although 15% of these examns. failed because of patient's movement during xenon gas inhalation. Blood flow in and around the brain tumor was measured in 37 patients with brain tumors (15 gliomas, 8 metastatic brain tumors, 14 meningiomas). A high flow area usually corresponded to that including viable tumor cells, while low flow area consisted of tissue with necrosis or brain edema. However, it was difficult to est. the invasive area of the tumor around the contrast enhanced lesion by Xe-CT. These areas were usually demonstrated as low flow area and was difficult to differentiate from necrosis or edema without tumor invasion. The changes of tumor blood flow under induced hypertension were examd. in 12 malignant brain tumor patients. Blood flow was measured before and after the induced hypertension, when blood pressure rose to nearly 140% of their initial blood pressure using ***angiotensin*** II drip infusion. Tumor blood flow increased 305 under induced hypertension in av. Autoregulation of the blood flow was not preserved in malignant brain tumors. Therefore, ***chemotherapy*** under the induced hypertensive state seems to be effective by increasing the drug delivery into the tumor tissue.

L6 ANSWER 4 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 95153801 MEDLINE
DOCUMENT NUMBER: 95153801 PubMed ID: 7850915
TITLE: Phase II study of a new combined primary chemotherapy regimen, intravenous methotrexate and vincristine and

intraarterial adriamycin and cisplatin, for locally advanced urinary bl[redacted]er cancer: preliminary results
AUTHOR: Kuroiwa T; Naito S; [redacted]asuo K; Kishikawa T; Masuda K; Kumazawa J
CORPORATE SOURCE: Department of Radiology, Kyushu University, Fukuoka, Japan.
SOURCE: CANCER CHEMOTHERAPY AND PHARMACOLOGY, (1995) 35 (5) 357-63. Journal code: 7806519. ISSN: 0344-5704.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950316

AB A phase II study of a new combination therapy was performed using intraarterial (i.a.) cisplatin and Adriamycin in combination with i.v. methotrexate and vincristine for 27 patients with invasive urinary bladder carcinoma of stages T2-3NOMO, and the therapeutic effects were assessed. Methotrexate (20 mg/m2) was given i.v. on days 1,15, and 22, and vincristine (0.7 mg/m2) was injected i.v. on day 2 before i.a. infusion therapy and on days 15 and 22. The i.a. ***chemotherapy*** was performed after both superior gluteal arteries had been embolized using 3- or 5-mm stainless-steel coils. A mixture of cisplatin (50-70 mg/m2) and Adriamycin (20 mg/m2) was infused i.a. via both internal iliac arteries over a period of 20-30 min. ***Angiotensin*** II (mean dose, 21 micrograms) was simultaneously infused i.a. in 15 of 27 patients. In 24 of the 27 patients, at least 2 cycles of full-dose ***chemotherapy*** were completed. The dose was decreased in the remaining 3 patients because of their poor health status and advanced age. Among the 27 patients, 9 and 14 had complete (CR) and partial responses (PR), respectively; 3 manifested no change (NC), and 1 had progressive disease (PD). The objective response rate (CR+PR) was 85.2%. Among the 27 patients staged T2-3 NOMO, 6 (CR, 1; PR, 5) underwent total cystectomies and 18 (CR, 8; PR, 8; NC, 2) had transurethral resection of a bladder tumor (TUR-Bt) or partial resections following ***chemotherapy*** . The remaining 3 diminished-dose patients had no surgery. Of the 27 patients, 22 were alive after a median follow-up period of 21+ (range, 7-48+) months. No significant ***side*** ***effect*** was observed except for lower extremity paresthesias in 5 patients (18.5%). These results point to the effectiveness of this therapy and to the possibility of urinary bladder preservation in patients with invasive, advanced urinary bladder cancers.

L6 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1995:111929 BIOSIS
DOCUMENT NUMBER: PREV199598126229
TITLE: Cardiovascular monitoring of drug-resistant lymphoma patients treated with EPOCH chemotherapy plus high does verapamil in continuous infusion.
AUTHOR(S): Tagliaferri, Pierosandro (1); Correale, Pierpaolo; Mottola, Michael; De Simone, Giovanni; Rea, Antonia; Ascione, Raimondo; Morabito, Aslessandro; Matano, Elide; Montesarchio, Vincenzo; Caraglia, Michael; Tortora, Giampaolo; Ciardiello, Fortunato; Barile, Carmen; Palmieri, Giovannela; Raffaele-Bianco, Angelo
CORPORATE SOURCE: (1) Cattedra Oncol. Med., Univ. Federico II Napoli, Via S. Pansini n.5, 80131 Napoli Italy
SOURCE: Oncology Reports, (1994) Vol. 1, No. 2, pp. 341-344.
DOCUMENT TYPE: Article
LANGUAGE: English

AB High dose Verapamil (VP) infusion has been incorporated into cytotoxic ***chemotherapy*** in order to circumvent tumor cell drug-resistance. We have evaluated the cardiovascular ***side*** - ***effects*** produced by high dose VP associated to EPOCH ***chemotherapy*** in 12 patients with chemorefractory lymphoma. Continuous monitoring of right ventricular and pulmonary pressure and cardiac index was performed in three patients by a Swan-Ganz catheter. A slight reduction in cardiac index was observed 6 h after the beginning of VP infusion and was followed by spontaneous recovery within 12 h. First degree atrioventricular (AV)

block was detected in 6/12 patients. Premature Ventricular Beats (PVB) occurred in one patient, and prompt disappeared after xylocaine administration. All patients experienced mild and transient hypotension, while severe hypotension was observed only in 1 patient, who promptly recovered when VP administration was discontinued. Hypokalemia was detected in 6 patients possibly as a consequence of transient activation of the renin- ***angiotensin*** system.

L6 ANSWER 6 OF 17 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 92272030 MEDLINE
DOCUMENT NUMBER: 92272030 PubMed ID: 1590270
TITLE: Intraarterial infusion chemotherapy with [Sar1,Ile8]angiotensin II for bladder cancer.
AUTHOR: Morita T; Kikuchi T; Hara Y; Ishikawa S; Kobayashi Y; Ishiyama S; Tozuka K; Goto K; Takahashi K; Yoshikawa H; +
CORPORATE SOURCE: Department of Urology, Jichi Medical School, Tochigi, Japan.
SOURCE: AMERICAN JOURNAL OF CLINICAL ONCOLOGY, (1992 Jun) 15 (3) 188-93.
Journal code: 8207754. ISSN: 0277-3732.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920623

AB Thirty-three patients with primary bladder cancer (nine stage T1 with multifocal tumors and 24 stage T2-4) were treated with intraarterial infusion ***chemotherapy*** including cisplatin, doxorubicin, and [Sar1,Ile8] ***Angiotensin*** II(AT II). Of the 32 evaluable patients, 12 had pathologically proven complete response (CR), 19 showed partial response (PR), and one showed no change (NC); the overall response rate (CR + PR) was 97%. The blood pressure increased in response to the administration of [Sar1,Ile8]AT II in all the patients; the mean increase in the systolic blood pressure was 36 mmHg. Most of the ***side*** ***effects*** were mild to moderate in severity, transient in nature, and included nausea/vomiting (100%), alopecia (84%), leukopenia (66%), headache (9%), nephrotoxicity (6%), diarrhea (3%), skin pigmentation (3%), and neurotoxicity (3%). One patient who dropped out of the study developed hemiplegia as a result of cerebral infarction. The findings indicate that it is necessary to exercise caution in selecting the patients to be subjected to this therapy. We conclude that intraarterial infusion ***chemotherapy*** combined with a vasoconstrictor has a significant effect not only against multifocal superficial bladder cancer but also against invasive bladder cancer.

L6 ANSWER 7 OF 17 MEDLINE
ACCESSION NUMBER: 92082261 MEDLINE
DOCUMENT NUMBER: 92082261 PubMed ID: 1746966
TITLE: Evaluation of induced hypertension chemotherapy (IHC) in ambulatory cancer patients.
AUTHOR: Sato H; Sugiyama K; Ishizuka K; Hoshi M; Urushiyama M
CORPORATE SOURCE: Dept. Clinical Cancer Chemotherapy, Research Institute for Cancer and Tuberculosis, Tohoku University, Sendai, Japan.
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1991 Dec) 18 (15) 2509-16.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199201
ENTRY DATE: Entered STN: 19920202
Last Updated on STN: 20000303
Entered Medline: 19920114

AB To evaluate ambulatory cancer ***chemotherapy*** (ACC), the clinical response, dose intensity of anticancer drugs, toxicities, ambulatory periods (AP) and survival days (SD) were analysed among 20 outpatients with various types of advanced cancer who were continuously treated by ***angiotensin*** II-IHC for the past 10 years. ACC was assessed with a

questionnaire by the patients themselves or their families. In advanced cancer, at first, it was essential to obtain a get clinical response or to stabilize the condition for a while, and secondly, to upgrade the performance status in better grade. Although AP and SD were so differed with the individuals: AP/SD = 1692.2 +/- 1450.2 days/2075.0 +/- 1348.0 days for CR (n = 5); 1086.0 +/- 1160.2 days/1344.3 +/- 1143.7 days for PR (n = 10); and 197.3 +/- 129.2 days/471.7 +/- 362.5 days for PD (n = 3). Alopecia, nausea/vomiting and appetite loss were the most frequent ***side*** ***effects*** , though these were almost completely controllable by ACC. Patients and their families could be cooperated and allow receiving ACC. The key in fighting cancer is the formation of good human relationship between medical oncologists and patients (including their families) mutual confidence, and giving a sufficient explanation for therapies.

L6 ANSWER 8 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 92151708 MEDLINE
DOCUMENT NUMBER: 92151708 PubMed ID: 1664635
TITLE: Angiotensin-induced hypertension chemotherapy in children with advanced solid tumors.
AUTHOR: Fujii Y; Hongo T; Masui H; Chiba T; Furukawa N; Nakajima H; Nasuda K; Yajima S; Horikoshi Y; Igarashi Y
CORPORATE SOURCE: Department of Pediatrics, Hamamatsu University School of Medicine, Shizuoka, Japan.
SOURCE: ACTA PAEDIATRICA JAPONICA, (1991 Jun) 33 (3) 381-3.
Journal code: 0370357. ISSN: 0374-5600.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920319
AB ***Angiotensin*** -induced hypertension ***chemotherapy*** (IHC) was investigated in six children with the following advanced malignancies: hepatocellular carcinoma, extraskeletal Ewing's sarcoma, sacrococcygeal malignant teratoma, small round cell tumor of the chest wall, hepatoblastoma and osteogenic sarcoma. Partial response was achieved in three of these patients, two showed no change, and in one IHC was used as adjuvant ***chemotherapy*** . The ***side*** ***effects*** of IHC were minimal and tolerable. ***Angiotensin*** -IHC may provide a new approach to pediatric cancer ***chemotherapy*** .

L6 ANSWER 9 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 92028175 MEDLINE
DOCUMENT NUMBER: 92028175 PubMed ID: 2130794
TITLE: Clinical evaluation of chemotherapy under angiotensin II-induced hypertension in patients with advanced cancer.
AUTHOR: Yamaue H; Tanimura H; Terashita S; Iwahashi M; Tani M; Tsunoda T; Tamai M; Mori K
CORPORATE SOURCE: Department of Gastroenterological Surgery, Wakayama Medical College.
SOURCE: NIPPON GEKA HOKAN. ARCHIV FUR JAPANISCHE CHIRURGIE, (1990 Jul 1) 59 (4) 302-9.
Journal code: 0421143. ISSN: 0003-9152.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 20000303
Entered Medline: 19911107
AB The clinical efficacy and indications for ***Angiotensin*** II (AT II)-induced hypertension ***chemotherapy*** were evaluated as a drug delivery system in 101 patients with advanced carcinoma. The sites of primary tumor studied included stomach (44), pancreas (18), colon (16), esophagus (6), bile duct (4), liver (3), breast (7) and 3 other single organs. Seventy four cases had distant metastases (lymph node (25), liver (29), peritoneum (16), and lung (4)). Additionally, the protocol was used 12 cases as postoperative adjuvant ***chemotherapy*** and 15 cases

following exploratory laparotomy. The blood pressure was elevated to a level 1.5 times base-line. The regimens used consisted of MMC + ADR (5), FAM (38) and CDDP (8). The dosages administered were MMC 7 mg/m2, ADR 14 mg/m2 and 5-FU 350 mg/m2. The cancer ***chemotherapy*** protocol with AT II was repeated for an average of 2.6 cycles with a 2-3 week interval. The drug concentration in tumor tissues was increased 1.7 fold by AT II treatment. The response rate was 15.8% (CR 7 and PR 9), and in those patients with lymph node, liver and peritoneal metastases was 48.0, 6.9 and 6.3%, respectively. The serum levels of tumor markers decreased in 9 patients. Subjective symptoms, such as hoarseness, edema and pain, were improved. The mean survival in patients with distant metastasis who responded was 343 days, and in nonresponders was only 168 days (p less than 0.05). The ***side*** ***effects*** of this therapy were slight, typically being grade 1 and 2. Thus, the chemotherapeutic agents studied in conjunction with AT II were effective in patients with lymph node metastasis. Additionally, this regimen could be performed safely with minimal ***side*** ***effects*** .

L6 ANSWER 10 OF 17 MEDLINE
ACCESSION NUMBER: 90025160 MEDLINE
DOCUMENT NUMBER: 90025160 PubMed ID: 2802636
TITLE: Intra-arterial infusion chemotherapy with [Sar1, Ile8] angiotensin II in bladder cancer.
AUTHOR: Morita T; Kikuchi T; Hara Y; Ishikawa S; Kobayashi Y; Ishiyama S; Tozuka K; Goto K; Nakashima N; Takahashi K; +
CORPORATE SOURCE: Dept. of Urology, Jichi Medical School, Tochigi, Japan.
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1989 Oct) 16 (10) 3417-22.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19891122
AB Twenty patients with bladder cancer were treated with intra-arterial infusion ***chemotherapy*** using CDDP and ADM in combination with [Sar1, Ile8] ***angiotensin*** II. A catheter was introduced into internal iliac artery by Seldinger's technique, and 100 mg of CDDP, 50 mg of ADM and 1 mg of [Sar1, Ile8] ***angiotensin*** II were infused through the catheter for 40 minutes. CR was observed in 8 of 20 patients. PR in 11 and NC in 1. Therefore, the response rate (CR + PR) was 95% (19/20). ***Side*** ***effects*** were generally mild and consisted of leukopenia, nausea, vomiting, diarrhea, alopecia, skin pigmentation and headache. Catheter-related complications were not observed. This study demonstrated that intra-arterial infusion ***chemotherapy*** with CDDP and ADM in combination with [Sar1, Ile8] ***angiotensin*** II was extremely effective in treating patients with bladder cancer.

L6 ANSWER 11 OF 17 MEDLINE
ACCESSION NUMBER: 89272076 MEDLINE
DOCUMENT NUMBER: 89272076 PubMed ID: 2543322
TITLE: Angiotensin II-induced hypertension chemotherapy of bone and soft-tissue sarcomas.
AUTHOR: Tsuchiya H; Tomita K; Sugihara M; Shimizu H; Yasutake H; Morishita H; Morikawa S; Ohno M; Bunko H; Seto M
CORPORATE SOURCE: Dept. of Orthopedic Surgery, Kanazawa University, School of Medicine.
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1989 Apr) 16 (4 Pt 2-3) 1776-81.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890623

AB We treated 14 patients with high grade sarcomas by ***angiotensin*** II-induced hypertension ***chemotherapy*** . The ***chemotherapy*** protocol described by Rosen was selected according to histological classification of sarcomas (small cell sarcoma, spindle cell sarcoma, pleomorphic sarcoma). The level of ***angiotensin*** -induced hypertension was one and half times as high as blood pressure at rest. Induced hypertension was maintained for 30-60 minutes. In three cases of 5 primary osteosarcomas, induced hypertension resulted in the increase of tumor stain and/or vascularity angiographically, and chemotherapeutic effects were CR or PR. The six cases with soft-tissue sarcomas were 2 cases each of CR, PR, and NC. The decrease of relative tumor blood flow under the condition of ***angiotensin*** II-induced hypertension was detected in 5 cases of 6 soft-tissue sarcomas by 133Xe clearance method. In the case of rhabdomyosarcoma, the decrease of tumor stain and vascularity by induced hypertension was observed on angiogram. As the ***side*** ***effects*** accompanying induced hypertension, nausea and chest oppression were noted in 2 cases, respectively. In this study it was suggested that ***angiotensin*** II-induced hypertension ***chemotherapy*** was effective for osteosarcoma, but that it might be ineffective for soft-tissue sarcomas.

L6 ANSWER 12 OF 17 MEDLINE
ACCESSION NUMBER: 89149125 MEDLINE
DOCUMENT NUMBER: 89149125 PubMed ID: 2645833
TITLE: Intra-arterial infusion chemotherapy: clinical applications and current status of therapeutic effects on various malignant tumors.
AUTHOR: Itsubo M; Kameda H
CORPORATE SOURCE: First Dept. of Internal Medicine, Jikei University School of Medicine.
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1989 Feb) 16 (2) 199-206. Ref: 32
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890404
AB Intra-arterial infusion ***chemotherapy*** for various malignant tumors in order to improve the antitumor effects and to diminish the ***side*** ***effects*** has been performed in general since the 1950's. Numerous reports have shown favourable therapeutic effects followed by the development of the new anticancer agents. Although in recent years application of intra-arterial administration of anticancer agents alone has been limited to such target tumors as liver cancer because of application of mechanical arterial embolization using gelatin sponge cubes, attempts have been made to enhance the antitumor effect. In order to improve targeting and stagnancy of anticancer agents in the tumor area, drug delivery systems involving arrangement of the hemodynamics of the tumor area (balloon-occluded arterial infusion therapy, administration with vasoconstrictive agents such as noradrenaline or ***angiotensin*** II and/or as administration with various drug carriers (microcapsules, lipiodol, albumin microspheres, Degradable Starch Microspheres, liposomes, etc.) have been prepared and made available for clinical use with various tumors. Furthermore, development of totally implantable equipment of intra-arterial use for not only continuous infusion but one-shot injection of anticancer agents contributes to the treatment of patients longer and more frequently with less trouble. In the future intra-arterial infusion ***chemotherapy*** will have an important role for treatment of various malignant tumors, especially as one part of multimodal treatments, although the pharmacokinetics should be more fully-studied.

L6 ANSWER 13 OF 17 MEDLINE
ACCESSION NUMBER: 88182285 MEDLINE
DOCUMENT NUMBER: 88182285 PubMed ID: 2451473
TITLE: Hepatic artery infusion chemotherapy with cisplatin and adriamycin in combination with angiotensin-II in the

treatment of malignant liver tumors.
AUTHOR: Morita S; Matsumoto [redacted] Odani R
CORPORATE SOURCE: Dept. of Radiology, Kochi Municipal Central Hospital.
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1988 Apr) 15 (4 Pt 1) 689-95.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198805
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19960129
Entered Medline: 19880510

AB Hepatic arterial infusion ***chemotherapy*** with cisplatin (CDDP) and adriamycin (ADR) in combination with ***angiotensin*** -II (AT-II) was performed in 19 cases of hepatocellular carcinoma (HCC), 16 cases of metastatic liver tumor (MLT) and one case of cholangiocellular carcinoma. CDDP (60-120 mg) and ADR (20-50 mg) were infused into the hepatic artery with intra-arterial instillation of AT-II (0.5-1.5 microgram/min). Transcatheter arterial embolization (TAE) was additionally performed in 10 cases of HCC and 3 cases of MLT. The response rates for infusion ***chemotherapy*** combined with TAE were 44% in HCC and 67% in MLT. On the other hand, the response rates without TAE were 0% in HCC and 42% in MLT. In some cases of HCC, however, a marked decrease in serum alpha-fetoprotein levels was observed despite the lack of effectiveness evaluated by CT scan and angiography. Although minor ***side*** ***effects*** were noted such as a mild degree of leukocytopenia and/or thrombocytopenia and hepatic and/or renal dysfunction, they were only temporary with a duration of less than 3 or 4 weeks. In 4 patients with HCC without TAE treatment, however, lethal ***side*** ***effects*** occurred including pancytopenia, hepatic failure and disseminated intravascular coagulation, and they died within 2 months after infusion ***chemotherapy*** . Renal failure was not seen in either group.

L6 ANSWER 14 OF 17 MEDLINE
ACCESSION NUMBER: 87183581 MEDLINE
DOCUMENT NUMBER: 87183581 PubMed ID: 3566300
TITLE: Two-route chemotherapy using the anticancer drug cis-diamminedichloroplatinum(II) and its antidote, sodium thiosulfate.
AUTHOR: Kuroiwa T; Baba T
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1987 Apr) 14 (4) 1011-7.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198705
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19900303
Entered Medline: 19870513

AB We described the efficacy of "two-route ***chemotherapy*** (TRC)", in which the anticancer drug, cis-diamminedichloroplatinum (II) (DDP), is injected locally, in combination with its antidote, sodium thiosulfate (STS), given systemically. First, we tested the protective effect of sulfur-containing compounds against DDP toxicity, and found STS to be the most potent antidote of DDP. On the basis of this finding, we developed TRC using DDP and STS, and applied it for liver and lung metastasis, bladder cancer, and peritoneal disseminated tumors in experimental animals, resulting in remarkable antitumor effects without serious ***side*** ***effects*** , especially nephrotoxicity. Furthermore, we obtained an optimal increase in the lifespan of rats bearing limb tumors when we tried TRC in combination with the ***angiotensin*** II (AT-II)-induced hypertension method. We also clarified that the protection of STS against DDP toxicity was mainly due to the diminution of the active platinum level in blood. We briefly reviewed the clinical trials of TRC, and discussed the improvements which still have to be made.

L6 ANSWER 15 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1987:170063 BIOSIS

DOCUMENT NUMBER: BA83:88504
TITLE: PREOPERATIVE INTRA-[redacted]ERIAL INFUSION CHEMOTHERAPY FO[redacted] ADVANCED BREAST CANCER.
AUTHOR(S): ABE H
CORPORATE SOURCE: DEP. OF SURGERY I, SCH. OF MED., IWATE MED. UNIV., MORIOKA, JAPAN.
SOURCE: J IWATE MED ASSOC, (1986 (RECD 1987)) 38 (4), 471-482. CODEN: IIZAAX. ISSN: 0021-3284.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese

AB During the period from 1982 through 1984, twenty patients with advanced breast cancer of Stage III and IV (TNM classification) were treated with preoperative intra-arterial infusion ***chemotherapy*** and radical mastectomy. For the purpose of preoperative intra-arterial infusion, two catheters were inserted in the subclavian artery via the superficial cervical artery and internal mammary artery via the superiorepigastric artery, respectively. Twenty patients were divided into four groups according to the administered drugs. Group 1: 6 patients administered Adriamycin (ADM) alone. Group 2: 6 patients administered ADM and 5-fluorouracil (5 FU). Group 3: 4 patients administered ADM with a infusion ***Angiotensin*** II (AT II) through the peripheral vein. Group 4: 4 patients administered ADM and 5 FU with use of AT II. ADM was given three times during 9 days in a 4 groups and total dose of ADM was 150 mg, and 250 mg of 5 FU was given every day in the Group 2 and the Group 4. After blood pressure was elevated by using AT II, ADM was administered through intrarterial catheter for 5 minutes in the Group 3 and the Group 4. Size of tumor and metastatic lymph nodes were measured, and reduction rate was calculated. Resected breast and lymph nodes were evaluated histologically according to Ohboshi and Shimosato's criterion. ***Side*** ***effects*** were also observed in the present study. The results were summarized as follows; 1) Reduction rate of all patients was 57.7 .+-. 26.3% in tumors and 68.9 .+-. 35.3% in lymph nodes, respectively. 2) There were no significant differences in the reduction rate among four groups. 3) Effective histological changes of the tumor were found in 61.1% of all patients, and that of the lymph nodes were found in 43.8%. 4) The most effective histological changes were observed in the Group 4. 5) ***Side*** ***effects*** frequently observed were gastro-intestinal disorder, stomatitis, dermatitis, alopetia, leukopenia and thrombocytopenia, but there were no patients who were discontinued the treatment because of ***side*** ***effects*** .

L6 ANSWER 16 OF 17 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 86135323 MEDLINE
DOCUMENT NUMBER: 86135323 PubMed ID: 3937720
TITLE: Hypertensive chemotherapy of advanced gastric cancer.
AUTHOR: Bai X W
SOURCE: CHUNG-HUA CHUNG LIU TSA CHIH [CHINESE JOURNAL OF ONCOLOGY], (1985 Sep) 7 (5) 380-1. Journal code: 7910681. ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 20000303
Entered Medline: 19860415

AB Hypertensive ***chemotherapy*** of advanced gastric cancer is reported in this paper. The blood pressure of the patient was first elevated by intravenous ***angiotensin*** II, then mitomycin C was given for two consecutive days at doses of 20 mg and 10 mg. Out of 20 cases, it was effective in 11 (55%), especially for those with Borrmann III and IV types and poorly differentiated adenocarcinoma which recurred after subtotal gastrectomy. The ***side*** ***effect*** of this treatment was not marked and the response satisfactory Therefore, it may easily be accepted as the treatment for advanced gastric cancer.

L6 ANSWER 17 OF 17 MEDLINE
ACCESSION NUMBER: 85120947 MEDLINE
DOCUMENT NUMBER: 85120947 PubMed ID: 4038597
TITLE: Intra-arterial infusion chemotherapy for non-resectable pancreatic cancer using angiotensin-II and

prostaglandin-E1.
AUTHOR: Ishikawa O; Ohhigas[redacted]H; Iwanaga T
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1985 Feb) 12 (2) 235-44.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198503
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850320

AB We have developed a new method of intra-arterial infusion ***chemotherapy*** for non-resectable pancreatic cancer, in order to facilitate the selective delivery of a large amount of anticancer agent to the cancer lesion. This method was carried out as follows: (1) retrograde cannulation was performed by inserting a catheter into the splenic artery after splenectomy, and many of its branches were dissected out around the body and tail of the pancreas: (2) anticancer drugs (Adriamycin and Methotrexate) were infused together with ***Angiotensin*** -II to decrease the blood flow to non-malignant tissue and to increase the flow to cancer tissue. (3) Twenty-four to 48 hours after Methotrexate was infused, rescue was performed with an infusion of Prostaglandin-E1 to reduce the degree of cytotoxic damage to normal tissue. By using these methods, it was ascertained that a large quantity of the drugs had accumulated in the cancer tissue, even though its original blood flow had been established as very poor by radioisotope and angiographical examination. This therapy was useful not only for anticancer effects on the primary lesion but also the prevention of liver metastasis. Moreover, Methotrexate and rescue therapy were shown to have no remarkable ***side*** ***effects*** .

=> d his

(FILE 'HOME' ENTERED AT 11:46:29 ON 18 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 11:46:54 ON 18 FEB 2003
L1 18020 S CHEMOTHERAPY (P) (SIDE EFFECT)
L2 297996 S ANGIOTENSINOGEN OR ANGIOTENSIN
L3 3606 S L2 (P) (FRAGMENT)
L4 29 S L1 (P) L2
L5 0 S L1 (P) L3
L6 17 DUPLICATE REMOVE L4 (12 DUPLICATES REMOVED)

=> s (hematopoietic toxicity) or (hematopoietic progenitor cell) or anemia or myelosuppression or
5 FILES SEARCHED...
L7 321749 (HEMATOPOIETIC TOXICITY) OR (HEMATOPOIETIC PROGENITOR CELL) OR ANEMIA OR MYELOSUPPRESSION OR PANCYTOPENIA

=> s thrombocytopenia or neutropenia or lymphopenia or leukopenia or stomatitis or alopecia or hea
L8 381376 THROMBOCYTOPENIA OR NEUTROPENIA OR LYMPHOPENIA OR LEUKOPENIA OR STOMATITIS OR ALOPECIA OR HEADACHE OR (MUSCLE PAIN)

=> s l2 (p) (l7 or l8)
L9 1085 L2 (P) (L7 OR L8)

=> s l3 (p) (l7 or l8)
L10 12 L3 (P) (L7 OR L8)

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L10
L11 9 DUPLICATE REMOVE L10 (3 DUPLICATES REMOVED)

=> s l11 not l6
L12 9 L11 NOT L6

=> d l12 1-9 ibib abs

L12 ANSWER 1 OF 9 MEDLINE
ACCESSION NUMBER: 1999060813 MEDLINE
DOCUMENT NUMBER: 99060813 PubMed ID: 9844823
TITLE: HELLP! A cry for laboratory assistance: a comprehensive review of the HELLP syndrome highlighting the role of the laboratory.
AUTHOR: Jones S L
CORPORATE SOURCE: Department of Pathology, Ball Memorial Hospital, Muncie, Indiana 47303, USA.
SOURCE: HEMATOPATHOLOGY AND MOLECULAR HEMATOLOGY, (1998) 11 (3-4) 147-71. Ref: 112
Journal code: 9608785. ISSN: 1082-8893.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990310

AB The HELLP syndrome is a dangerously severe form of preeclampsia associated with multiorgan system damage and occurs in 0.2-0.6% of all pregnancies. It usually presents with abdominal pain, often in the setting of preeclampsia. In most cases, HELLP is initiated by inadequate placental vessel development with subsequent placental ischemia, leading to the release of circulating vasoconstrictors. These powerful vasoconstrictors include thromboxane A2, ***angiotensin*** , prostaglandin F2, and endothelin-1. The ischemic placenta also produces fewer vasodilators, such as prostacyclin, prostaglandin, E2, and nitric oxide. The ensuing imbalance in vasoactive substances causes intense systemic vasospasm and multiorgan endothelial damage. Multiple genetic, coagulation, and immunologic disorders also appear to contribute to the endothelial damage. Fibrin and platelets are then deposited on the endothelial surfaces leading to the hemolytic ***anemia*** , elevated liver enzymes, and low platelets of the HELLP syndrome. The most reliable laboratory tests for the diagnosis of HELLP are a complete blood count with peripheral smear, lactate dehydrogenase, serum transaminases, and urinalysis. Supportive tests include serum haptoglobin, D-dimer ***fragment*** levels, lactate dehydrogenase isoenzymes, total bilirubin, prothrombin times, and activated partial thromboplastin times. Lactate dehydrogenase and the platelet count are the two best tests to monitor the course of the disease. Prompt delivery is the treatment of choice. The intensity of the HELLP syndrome peaks 24 hours after delivery. Extended atypical HELLP has been successfully treated with plasma exchange. The clinical laboratory professional plays an important role in the diagnosis, follow-up, and treatment of patients with the HELLP syndrome.

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:69631 CAPLUS
TITLE: Method for predicting the development of iron deficiency anemia (variants)
INVENTOR(S): Morozova, A. A.; Safuanova, G. Sh.; Khusnutdinova, E. K.; Chepurnaya, A. N.
PATENT ASSIGNEE(S): Bashkirskii Gosudarstvennyi Meditsinskii Universitet, Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| RU 2187812 | C1 | 20020820 | RU 2001-118895 | 20010706 |

PRIORITY APPLN. INFO.: RU 2001-118895 20010706

AB FIELD: medicine, hematol. SUBSTANCE: it is conducted the anal. of polymorphous loci of P 4501A1 cytochromic gene due to polymerase chain reaction of DNA synthesis, it is conducted in DNA isolated due to

phenol-chloroform extn. technique [redacted] of lymphocytes of peripheral venous blood. After amplification and ex[redacted] DNA ***fragments*** are [redacted] electrophoretically divided in 7%- polyacrylamide nondenaturated gel and analyzed under UV lighting by using a transulluminator: the presence of DNA- ***fragments*** at the size of 48 and 139 nucleotide pairs (np) is interpreted as isoleucin allele (Ile), at the size of 48, 120 and 19 np - as valine (Val). Relative risk of disease development (RR) is concluded on at RR>1.5. At revealing Ile/Val genotype it is predicted the risk of IDA development (variant 1). Then it is conducted the anal. of polymorphous loci of glutathione S-transferase M1 genes (GSTM1), N-acetyltransferase 2 (Nat2), ***angiotensin*** converting enzyme (ACE) and plasminogene activator (PA) due to the method of polymerase chain reaction of DNA synthesis (PCR) and at revealing genotype combinations of 0/0,S/R,I/D,I/D; +/+,R/R,I/I,I/D; +/+,S/S,I/D,I/D; +/+,S/R,I/I, I/D; +/+,S/R,D/D,I/I the risk of iron deficiency ***anemia*** development is predicted. EFFECT: higher accuracy of prediction. 2 cl, 2 ex, 1 tbl.

L12 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:935627 CAPLUS
DOCUMENT NUMBER: 136:48819
TITLE: Methods for treating and preventing ***alopecia*** using ***angiotensinogen*** , ***angiotensin*** I, ***angiotensin*** II, their analogs and ***fragments*** and AT2 receptor agonists
INVENTOR(S): Roders, Kathleen E.; Dizerega, Gere S.
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001098325 | A1 | 20011227 | WO 2000-US32340 | 20001127 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-212608P P 20000619
OTHER SOURCE(S): MARPAT 136:48819
AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing ***alopecia*** in a subject in need thereof by administering an effective amt. of ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogs, AI ***fragments*** and analogs thereof, ***angiotensin*** II (AII), AII analogs, AII ***fragments*** or analogs thereof or AII AT2 type 2 receptor agonists to the subject. The method further comprises treating the subject with an effective amt. of another compd. for treating or preventing ***alopecia*** , selected from the group consisting of minoxidol, keratinocyte growth factor, fibroblast growth factor, epidermal growth factor, butyric acid and its derivs., ammonium trichloro(dioxyethylene-O,O') tellurate, interleukin 1, prostaglandin E2, cyclosporine A, corticosteroids and calcitriol.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:452872 CAPLUS
DOCUMENT NUMBER: 135:56494
TITLE: Methods for treating and preventing damage to mucosal tissue using angiotensinogen, angiotensin I, AI analogs, AI fragments and analogs, angiotensin II, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists

INVENTOR(S): Rodgers, Kathl[redacted] E.; Dizerega, Gere S.
PATENT ASSIGNEE(S): University of [redacted]thern California, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001043761 | A2 | 20010621 | WO 2000-US32141 | 20001127 |
| WO 2001043761 | A3 | 20020307 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1239867 | A2 | 20020918 | EP 2000-980704 | 20001127 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

PRIORITY APPLN. INFO.: US 1999-171249P P 19991216
US 2000-213224P P 20000619
WO 2000-US32141 W 20001127

OTHER SOURCE(S): MARPAT 135:56494

AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing damage to mucosal tissue by administering an effective amt. of angiotensinogen, angiotensin I (AI), AI analogs, AI fragments and analogs thereof, angiotensin II (AII), AII analogs, AII fragments or analogs thereof or AII AT2 type 2 receptor agonists to the subject. Administration of anti-inflammatory drugs, angiotensin converting enzyme inhibitors, anti-infectives, growth factors, and/or antihistamines in combination with the above compns. is also claimed.

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:736492 CAPLUS
DOCUMENT NUMBER: 131:347095
TITLE: Methods to increase white blood cell survival after chemotherapy using angiotensinogen, angiotensin I or II and their fragments or analogs
INVENTOR(S): Rodgers, Kathleen; Dizerega, Gere
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9958140 | A1 | 19991118 | WO 1999-US10205 | 19990510 |
| W: AU, CA, JP, MX | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2322963 | AA | 19991118 | CA 1999-2322963 | 19990510 |
| AU 9939798 | A1 | 19991129 | AU 1999-39798 | 19990510 |
| EP 1073453 | A1 | 20010207 | EP 1999-922905 | 19990510 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6475988 | B1 | 20021105 | US 1999-307940 | 19990510 |

PRIORITY APPLN. INFO.: US 1998-84908P P 19980511
US 1998-92633P P 19980713
WO 1999-US10205 W 19990510

OTHER SOURCE(S): MARPAT 131:347095

AB The present invention provides improved methods, kits, and pharmaceutical compns. for increasing white blood cell survival following chemotherapy,

and mobilizing ***hematopoietic*** ***progenitor*** ***cells*** from bone marrow into peripheral blood, comprising the administration of an effective amt. of ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogs, AI ***fragments*** and analogs thereof, ***angiotensin*** II (AII), AII analogs, AII ***fragments*** or analogs thereof or AII AT2 type 2 receptor agonists.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:511174 CAPLUS
DOCUMENT NUMBER: 131:154024
TITLE: Method of promoting erythropoiesis with angiotensinogen, angiotensins, their analogs or fragments
INVENTOR(S): Rodgers, Kathleen E.; Dizerega, Gere
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9940106 | A2 | 19990812 | WO 1999-US2648 | 19990208 |
| WO 9940106 | A3 | 19990923 | | |
| W: AU, CA, JP, MX | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2319701 | AA | 19990812 | CA 1999-2319701 | 19990208 |
| AU 9925916 | A1 | 19990823 | AU 1999-25916 | 19990208 |
| EP 1053004 | A2 | 20001122 | EP 1999-905848 | 19990208 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6239109 | B1 | 20010529 | US 1999-245680 | 19990208 |
| JP 2002509077 | T2 | 20020326 | JP 2000-530534 | 19990208 |

PRIORITY APPLN. INFO.: US 1998-74106P P 19980209
US 1998-111535P P 19981209
WO 1999-US2648 W 19990208
OTHER SOURCE(S): MARPAT 131:154024
AB The present invention provides methods, compds., pharmaceutical compns., and kits for the augmentation of erythropoiesis by potentiating erythropoietin-induced differentiation with ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogs, AI ***fragments*** and analogs thereof, ***angiotensin*** II analogs, AII ***fragments*** or analogs thereof or AII AT2 type 2 receptor agonists as a therapeutic adjunct. The method is useful for the treatment of congenital or acquired aplastic or hypoplastic ***anemia*** assocd. with chronic renal failure, end-stage renal disease, renal transplantation, cancer, AIDS, chemotherapy, radiotherapy, bone marrow transplantation and chronic diseases. An improved cell culture medium for promotion of erythropoiesis is also claimed.

L12 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2003:32036 BIOSIS
DOCUMENT NUMBER: PREV200300032036
TITLE: Methods to increase white blood cell survival after chemotherapy.
AUTHOR(S): Rodgers, Kathleen E.; DiZerega, Gere
ASSIGNEE: University of Southern California
PATENT INFORMATION: US 6475988 November 05, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 5 2002) Vol. 1264, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention provides improved methods, kits, and pharmaceutical compositions for increasing white blood cell survival following

chemotherapy, and mobilizing ***[illegible]atopoietic*** ***progenitor*** ***cells*** from bone marrow i[illegible] peripheral blood, comprising administration of an effective amount of ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogues, AI ***fragments*** and analogues thereof, ***angiotensin*** II (AII), AII analogues, AII ***fragments*** or analogues thereof or AII AT2 type 2 receptor agonists.

L12 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:534172 BIOSIS
DOCUMENT NUMBER: PREV200100534172
TITLE: Method of promoting erythropoiesis.
AUTHOR(S): Rodgers, Kathleen E.; DiZerega, Gere
ASSIGNEE: University of Southern California
PATENT INFORMATION: US 6239109 May 29, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 29, 2001) Vol. 1246, No. 5, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention provides methods, compounds, pharmaceutical compositions, and kits for the augmentation of erythropoiesis by potentiating erythropoietin-induced differentiation with ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogues, AI ***fragments*** and analogues thereof, ***angiotensin*** II analogues, AII ***fragments*** or analogues thereof or AII AT2 type 2 receptor agonists as a therapeutic adjunct. The method is useful for the treatment of congenital or acquired aplastic or hypoplastic ***anemia*** associated with chronic renal failure, end-stage renal disease, renal transplantation, cancer, AIDS, chemotherapy, radiotherapy, bone marrow transplantation and chronic diseases.

L12 ANSWER 9 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78196138 EMBASE
DOCUMENT NUMBER: 1978196138
TITLE: Gaucher's disease, a review.
AUTHOR: Peters S.P.; Lee R.E.; Glew R.H.
CORPORATE SOURCE: Dept. Biochem., Univ. Pittsburgh Sch. Med., Pittsburgh, Pa. 15261, United States
SOURCE: Medicine, (1977) 56/5 (425-442).
CODEN: MEDIAV
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
AB Gaucher's disease is a lysosomal storage disease characterized by the accumulation of glucocerebroside in reticuloendothelial cells in bone marrow, spleen, and liver. Glucocerebroside, a complex glycolipid membrane ***fragment*** , accumulates because the enzyme responsible for its degradation, glucocerebroside: .beta.-glucosidase, is deficient in affected individuals. Clinically, Gaucher's disease presents in multiple forms. The most common variety of Gaucher's disease, the 'adult' form, often presents with hepatosplenomegaly, ***anemia*** , ***thrombocytopenia*** , and erosion of the cortices of the long bones. However, individuals with this form of Gaucher's disease display a wide variety of clinical severity, with some individuals being devastated by the disease by their third decade of life, and others leading relatively symptom-free lives for 7 or 8 decades. Individuals with the 'acute neuropathic' or 'infantile' form of Gaucher's disease display neurological as well as visceral involvement and usually die before 2 years of age. The reason for the variability in the clinical expression of Gaucher's disease is not clear, in addition, the extent of pathology does not always correlate with residual glucocerebrosidase activity determined by current methods. Investigation of the enzymology of Gaucher's disease has revealed that the activity of purified human glucocerebrosidase can be modified in vitro by a number of physiological compounds including phospholipids, gangliosides, phosphate ion, and certain glycoproteins. Gaucher's disease has also been shown to be associated with several other abnormalities that have no obvious relation to glucocerebroside metabolism. Individuals with

Gaucher's disease have been shown t[redacted]have increased levels of serum and splenic acid phosphatase activity, [redacted]creased iron stores, increased [redacted] ***angiotensin*** converting enzyme, and a relative factor IX deficiency. The possibility that various physiological compounds might alter glucocerebrosidase activity in vivo, and that some of these ancillary features of Gaucher's disease may contribute to pathology of the disease should be explored. These findings might help to explain some of the clinical heterogeneity observed in individuals with Gaucher's disease and could lead to improved approaches to the therapy of Gaucher's disease.

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(FILE 'HOME' ENTERED AT 11:46:29 ON 18 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 11:46:54 ON 18 FEB 2003

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L1         18020 S CHEMOTHERAPY (P) (SIDE EFFECT)
L2        297996 S ANGIOTENSINOGEN OR ANGIOTENSIN
L3          3606 S L2 (P) (FRAGMENT)
L4            29 S L1 (P) L2
L5             0 S L1 (P) L3
L6            17 DUPLICATE REMOVE L4 (12 DUPLICATES REMOVED)
L7        321749 S (HEMATOPOIETIC TOXICITY) OR (HEMATOPOIETIC PROGENITOR CELL) O
L8        381376 S THROMBOCYTOPENIA OR NEUTROPENIA OR LYMPHOPENIA OR LEUKOPENIA
L9          1085 S L2 (P) (L7 OR L8)
L10           12 S L3 (P) (L7 OR L8)
L11            9 DUPLICATE REMOVE L10 (3 DUPLICATES REMOVED)
L12            9 S L11 NOT L6
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=> s cytokine or (granulocyte colony stimulating factor) or (granulocyte macrophage csf) or (epide
   4 FILES SEARCHED...
L13      691294 CYTOKINE OR (GRANULOCYTE COLONY STIMULATING FACTOR) OR (GRANULOC
                YTE MACROPHAGE CSF) OR (EPIDERMAL GROWTH FACTOR)

=> s interleukin or thrombopoietin or (growth factor) or pixkines or (stem cell factor) or (flt li
   3 FILES SEARCHED...
   5 FILES SEARCHED...
L14     1296395 INTERLEUKIN OR THROMBOPOIETIN OR (GROWTH FACTOR) OR PIXKINES OR
                (STEM CELL FACTOR) OR (FLT LIGAND)

=> s (l6 or l12) (p) (l13 or l14)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L71) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L74) (P) '
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L77) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L80) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L83) (P) '
L15            3 (L6 OR L12) (P) (L13 OR L14)

=> d l15 1-3 ibib abs

L15  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:935627  CAPLUS
DOCUMENT NUMBER:          136:48819
TITLE:                    Methods for treating and preventing  ***alopecia***
                          using  ***angiotensinogen***  ,  ***angiotensin***
                          I,  ***angiotensin***  II, their analogs and
                          ***fragments***  and AT2 receptor agonists
INVENTOR(S):              Roders, Kathleen E.; Dizerega, Gere S.
PATENT ASSIGNEE(S):       University of Southern California, USA
SOURCE:                   PCT Int. Appl., 48 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001098325 | A1 | 20011227 | WO 2000-US32340 | 20001127 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-212608P P 20000619
OTHER SOURCE(S): MARPAT 136:48819

AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing ***alopecia*** in a subject in need thereof by administering an effective amt. of ***angiotensinogen*** , ***angiotensin*** I (AI), AI analogs, AI ***fragments*** and analogs thereof, ***angiotensin*** II (AII), AII analogs, AII ***fragments*** or analogs thereof or AII AT2 type 2 receptor agonists to the subject. The method further comprises treating the subject with an effective amt. of another compd. for treating or preventing ***alopecia*** , selected from the group consisting of minoxidol, keratinocyte ***growth*** ***factor*** , fibroblast ***growth*** ***factor*** , ***epidermal*** ***growth*** ***factor*** , butyric acid and its derivs., ammonium trichloro(dioxyethylene-O,O') tellurate, ***interleukin*** 1, prostaglandin E2, cyclosporine A, corticosteroids and calcitriol.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:452872 CAPLUS
DOCUMENT NUMBER: 135:56494
TITLE: Methods for treating and preventing damage to mucosal tissue using angiotensinogen, angiotensin I, AI analogs, AI fragments and analogs, angiotensin II, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists
INVENTOR(S): Rodgers, Kathleen E.; Dizerega, Gere S.
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001043761 | A2 | 20010621 | WO 2000-US32141 | 20001127 |
| WO 2001043761 | A3 | 20020307 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| EP 1239867 | A2 | 20020918 | EP 2000-980704 | 20001127 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 1999-171249P P 19991216
US 2000-213224P P 20000619
WO 2000-US32141 W 20001127

OTHER SOURCE(S): MARPAT 135:56494

AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing damage to mucosal tissue by

administering an effective amt. of angiotensinogen, angiotensin I (AI), AI analogs, AI fragments and analogs thereof, angiotensin II (AII), AII analogs, AII fragments or analogs thereof or AII AT2 type 2 receptor agonists to the subject. Administration of anti-inflammatory drugs, angiotensin converting enzyme inhibitors, anti-infectives, ***growth*** ***factors*** , and/or antihistamines in combination with the above compns. is also claimed.

L15 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000169962 EMBASE
TITLE: Neoral use in the cardiac transplant recipient.
AUTHOR: Valantine H.
CORPORATE SOURCE: Dr. H. Valantine, Stanford University Hospital, CVRC, Heart/Lung Transplantation Division, Palo Alto, CA 94305, United States
SOURCE: Transplantation Proceedings, (2000) 32/3 SUPPL. 1 (27S-44S).
Refs: 80
ISSN: 0041-1345 CODEN: TRPPA8
PUBLISHER IDENT.: S 0041-1345(00)00862-9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Special Considerations in the Cardiac Transplant Patient: CyA is the core immunosuppressant of choice for the majority of transplant patients. The introduction of Neoral, a new microemulsion formulation of CyA, and more recently a range of adjunctive immunosuppressants have further enhanced the efficacy and tolerability of CyA-based immunosuppression. In the first year following transplantation the major causes of morbidity and death are graft failure, acute rejection, and systemic infection. Patients with deteriorated pulmonary circulation before transplantation are at increased risk of early postoperative death. Risk factors for early acute rejection include female donor sex, young donor age, and multiple HLA-DR mismatches. The principal cause of death in the long term is graft vasculopathy which accounted for 40% of all deaths. Risk factors that have been hypothesized to play a role in the pathogenesis of graft vasculopathy 4 include hyperlipidemia, recipient age and gender, donor age, the number of HLA AB and DR mismatches, and CMV infection. Strategies proposed to reduce the risk of graft vasculopathy include aggressive use of lipid-lowering agents, avoidance of low CyA doses, and the use of adjunctive rapamycin or RAD therapy. Rejection surveillance therefore relies on routine serial endomyocardial biopsy. Recent research suggests that a more accurate assessment of the state of the graft can be obtained by considering the results across a number of biopsy samples obtained from different parts of the heart, rather than basing clinical judgment on the worst single result obtained. New molecular markers such as granzyme A mRNA are likely to improve the power of histology to diagnose and predict rejection. Neoral Immunosuppression in De Novo Patients: Neoral pharmacokinetics give greater bioavailability and less intrapatient variability than Sandimmune. In the keynote OLN 351 study comparing Neoral with Sandimmune in de novo heart transplant recipients, fewer Neoral patients needed antilymphocyte therapy to treat rejection, fewer female patients had rejection episodes in the Neoral group, the tolerability of the two formulations was equivalent, and there was a lower incidence of infections in the Neoral group. The clinical impact of Neoral in comparison with Sandimmune in de novo heart transplant patients has been investigated in a number of additional trials, including long-term studies, which have confirmed that Neoral is associated with: Lower CyA doses than Sandimmune. Equal or greater antirejection efficacy than Sandimmune. Comparable tolerability to Sandimmune. During the administration of intravenous CyA as an induction therapy in the days immediately following transplantation, there is evidence to suggest that a 6-hour infusion given twice daily, which mimics the pharmacokinetic profile of oral dosing, may be clinically more effective than a continuous 24-hour infusion. Neoral Immunosuppression in the Maintenance Patient: Milligram-for-milligram dose conversion from Sandimmune to Neoral is feasible. Following conversion, a reduction in the

CyA dose may be required in the majority of patients to maintain target levels. In pediatric patients, the rate of elimination of CyA is greater and bioavailability increases with increasing age. Younger patients (less than 8 years of age) may be managed more effectively with a 3-times-daily, rather than a twice-daily dosing schedule. A number of studies have compared the clinical effects of Sandimmune and Neoral in maintenance therapy for cardiac transplant patients. As with de novo patients, these studies have found the new formulation of CyA to be associated with lower rates of acute rejection, lower therapeutic doses, and comparable tolerability. Milligram-to-milligram conversion from the old to the new CyA formulation is generally well tolerated, although in a minority of patients there is a significant increase in CyA levels. These may be associated with a transient increase in ***side*** ***effects*** which resolve on dose reduction. There is a dose-sparing effect with Neoral. Routine monitoring of both CyA and serum creatinine levels are advisable to optimize the tolerability and safety of therapy. Recent research indicates that drug monitoring 2 hours after CyA dosing provides a more accurate indication of AUC than trough level measurements. Patients with persistently low CyA levels are likely to be at increased risk of graft loss due to both acute rejection and chronic graft vasculopathy. New evidence suggests the use of C-2 CyA level monitoring to determine whether adequate drug is being absorbed. This TDM approach is not only recommended as a diagnostic tool but as a method for optimising Neoral immunosuppression. Long-term ***Side*** ***Effects*** of CyA Therapy: The major long-term safety problems directly associated with CyA-based immunosuppression include nephrotoxicity, hypertension, diabetes mellitus, and PTLD. CyA nephrotoxicity No clear risk factors for CyA nephrotoxicity have been identified and no correlation has been observed between CyA levels and serum creatinine levels. Overactivation of the renin- ***angiotensin*** system may play a role in the development of CyA nephrotoxicity, in which case early introduction of an ACE inhibitor would be expected to be of benefit. This possibility has yet to be investigated in a clinical trial. Reducing the CyA dose to treat renal dysfunction should be carried out with care, because this increases the risk of acute rejection. The introduction of additional, non- nephrotoxic adjunctive therapies such as MMF should be considered when substantially reducing the CyA dose. Hypertension: Management of hypertension requires careful attention to dietary sodium intake. Reducing the dose of CyA - as well as steroids, which also contribute to the problem - is important although care must be taken to avoid increasing the risk of rejection. The use of nonsteroidal anti-inflammatory agents should be avoided in hypertensive patients receiving CyA, because this may lead to further impairment of renal function. Because hypertension is often at its greatest in the early morning in cardiac transplant patients and the normal diurnal variation in blood pressure is absent, optimal management is often achieved by giving larger doses of antihypertensive agents at bedtime. PTLD: The optimal treatment for PTLD has not yet been determined, but strategies involving a reduction of immunosuppression in combination with aggressive ***chemotherapy*** have reported significant success. Prophylactic use of antiviral therapy is also recommended. Diabetes and Steroid Withdrawal: Steroid-sparing protocols are an important strategy for reducing posttransplant diabetes and should especially be considered in patients judged on the basis of preoperative metabolic parameters to be at a high risk of developing diabetes. Although steroid-sparing protocols are undoubtedly beneficial to many patients receiving immunosuppression with CyA or other agents, there is continuing debate over the clinical benefits of complete steroid withdrawal. Adjunct Immunosuppression Agents: Although CyA remains the cornerstone of maintenance immunosuppression therapy, the use of new adjunctive agents can reduce the risk of rejection; enable lower, better-tolerated doses of CyA and steroids to be administered; and enable therapy to be better tailored to clinical needs. Simulect (basiliximab) and daclizumab induction therapy within a CyA-based protocol has been shown to be highly effective in reducing the incidence of early acute rejection episodes in two major trials in renal transplantation, and similar results are anticipated in heart transplantation. Substitution of MMF for azathioprine reduces the frequency and severity of acute rejection episodes, may delay the development of chronic graft vasculopathy, and may improve patient survival in CyA-treated heart transplant patients. Sirolimus (rapamycin) and RAD have complementary mode of action to CyA. Early indications are that they offer significant clinical benefits in heart transplantation, including reduced rejection rates, lower CyA toxicity through reduced

doses, and possibly a reduced incidence of chronic graft vasculopathy. Tacrolimus has a similar mode of action to CyA and the two agents should not be used in combination. In terms of clinical outcomes, no clear advantage has been demonstrated for either agent in comparison with the other. However, in some circumstances it may be appropriate to switch patients from CyA to tacrolimus-based therapy or vice versa, either to treat refractory rejection in CyA patients, or to treat severe tacrolimus toxicity. A range of options is available for the treatment of acute rejection; these options vary according to rejection severity and persistence. Many of these use adjunctive immunosuppressants including MMF, rapamycin, or RAD.

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(FILE 'HOME' ENTERED AT 11:46:29 ON 18 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 11:46:54 ON 18 FEB 2003

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L1         18020 S CHEMOTHERAPY (P) (SIDE EFFECT)
L2        297996 S ANGIOTENSINOGEN OR ANGIOTENSIN
L3          3606 S L2 (P) (FRAGMENT)
L4            29 S L1 (P) L2
L5             0 S L1 (P) L3
L6            17 DUPLICATE REMOVE L4 (12 DUPLICATES REMOVED)
L7        321749 S (HEMATOPOIETIC TOXICITY) OR (HEMATOPOIETIC PROGENITOR CELL) O
L8        381376 S THROMBOCYTOPENIA OR NEUTROPENIA OR LYMPHOPENIA OR LEUKOPENIA
L9          1085 S L2 (P) (L7 OR L8)
L10           12 S L3 (P) (L7 OR L8)
L11            9 DUPLICATE REMOVE L10 (3 DUPLICATES REMOVED)
L12            9 S L11 NOT L6
L13       691294 S CYTOKINE OR (GRANULOCYTE COLONY STIMULATING FACTOR) OR (GRANU
L14      1296395 S INTERLEUKIN OR THROMBOPOIETIN OR (GROWTH FACTOR) OR PIXKINES
L15            3 S (L6 OR L12) (P) (L13 OR L14)
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=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 135.13 | 135.34 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -5.21 | -5.21 |

STN INTERNATIONAL LOGOFF AT 12:01:15 ON 18 FEB 2003